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Development of Medical Adjunctive Treatment for Acute Penetrating Head Injury

Annual Report

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Patients have been divided into two separate groups: (1) those who are in deep coma (Glasgow Coma Score (GCS) 3-5, and (2) those in light coma or awake, GCS 6-15. Although patients with an initials GCS 3-5 have a very poor prognosis (98% fatality), there is still considerable controversy nationwide over their management, particularly with regard to early surgery. The P.I. has thus chosen a factorial design to address two questions simultaneously on the same group of GCS 3-5 patients: the value of early surgery in this group, and the value of PEG-SOD. GCS 6-15 patients will all undergo early surgery and then be entered in the PEG-SOD trial. All patients participating in the trial are expected to benefit from it, since they will all receive intensive standardized ICU care. Keywords:)

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FOREWORD

For the protection of human subjects, the investigator(s) have adhered to policies of applicable Federal Law 45CFR56.

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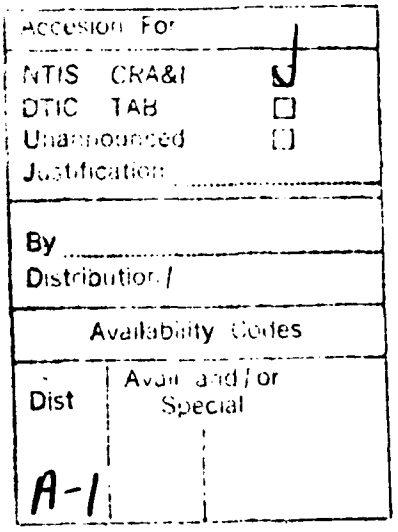

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NEUROLOGY

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ANNUAL REPORT (1 October 1987-31 October 1988)
ARMY PENETRATING HEAD INJURY PROJECT (APHIP), 87PP7824
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Since the Annual report of the Army Penetrating Head Injury Project (APHIP) submitted in November 1987, the following has been accomplished:

1. A standardized, multicenter (four centers) system has been established for conducting sequential therapeutic trials on head injured patients.

2. The pretreatment pilot phase of the program has been completed, including computerized data transmission to WRAMC. One hundred and twenty-four penetrating head injured patients have been treated at the participating hospitals since 1 January 1988. Data entry forms and procedures have been pretested on 41 of them; appropriate modifications to the forms and to the supporting computer system have now been completed. A revised version of the APHIP Manual was forwarded to Commander, LAIR, in October 1988.

3. Local medical center, USUHS, and Army Surgeon General Human Use approvals have been obtained for a clinical trial of PEG-Superoxide Dismutase (PEG-SOD) and surgery in head injured patients.

4. Enzon, Inc., who had originally committed to supply the PEG-SOD for the trial has sold its rights to the drug to Eastman Pharmaceuticals. Eastman Pharmaceuticals has agreed to honor the original commitment to the APHIP. Final arrangements are currently underway with them to begin patient randomization.

Since initial protocol submission early this year to the six review boards involved, additional experimental data has become available more strongly supporting a potential therapeutic role for PEG-SOD in the management of both closed and penetrating head injury. At the request of Eastman Pharmaceuticals, we have agreed to make two modifications to our protocol, (a) an increase in the dosage of PEG-SOD to be used (based on very recent, as yet unpublished animal and human testing by other groups), and (b)

inclusion of patients with severe closed head injuries, to be stratified-randomized separately into the study. We believe that both of these modifications are in the best interests of the APHIP, and can be accomplished in our system without any further increases in funding. The APHIP is currently the only group in the nation poised to begin SOD trials in any head injured patients; other groups have similar studies in planning stages.

5. A national survey of penetrating head injury (PHI) management practices of 3000 neurosurgeons has been completed, with a 36% return of questionnaires. Preliminary analysis shows a wide variability in neurosurgical management of PHI throughout the nation, and brings into question some fundamental elements of the present official US Army standard of care for PHI. Final analyses are now underway, and will be forwarded as soon as they are completed.

GOALS FOR FY 89

1. To begin formal clinical trial of PEG-SOD and acute intracranial surgery in head injury; accession rate goal: 100 patients per year.

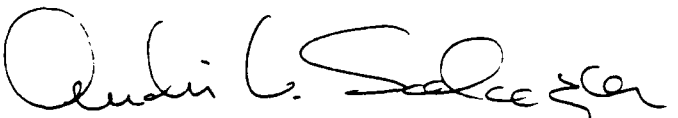
2. To further refine the multicenter system, including better definition of outcome parameters for therapeutic trials in head injury.

3. Depending on preliminary results of current trial, to identify potential therapeutic strategies for future human trials.

GOALS FOR FY 90

1. To continue accessions into the SOD clinical trials.

2. To recruit additional medical centers into the system (dependent on funding).



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